

# ANTIMICROBIALS – WHO NEEDS THEM?

A Roundtable Event, Chaired by FAI in partnership with Ceva

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## ANTIMICROBIAL RESISTANCE ROUNDTABLE REPORT



## PARTICIPANTS (CHATHAM HOUSE RULES APPLY)

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## AIMS OF THE ROUNDTABLE

In the face of growing human health problems associated with antimicrobial resistance a group of veterinarians, food scientists, farmers and representatives from the food and animal health industries came together for a Roundtable discussion. The aims of the meeting were to explore ways forward to effectively and responsibly manage antimicrobial use in food production in a way that decelerates the development of resistance in both humans and animals, protects animal welfare, and ensures our ability to feed the world in a safe and sustainable manner.

## SETTING THE SCENE

Resistance describes the ability of certain bacteria to resist the effects of antimicrobial therapy. Antimicrobial use in humans is likely to be a major driver. The participants agreed that while the level of contribution of animal agriculture to the increasing problems of antimicrobial resistance in humans may be difficult to quantify, there are without doubt links between the use of antimicrobials in humans and animals. This relationship is recognised globally and there is growing consensus and pressure concerning the need to move towards more responsible use of antimicrobials in food-producing animals, in order to decelerate the development of resistance both in humans and animals.

## EFFECTING CHANGE

A topic of interest to the participants of the Roundtable was the ways and means available to effect change in current practice and use of antimicrobials in food producing animals. Three main areas were highlighted: legislative reform; behavioural change; and system change.

### Legislative Reform

It appears that new European legislation for use of Critically Important Antimicrobials (CIAs) in agriculture is in the pipeline and is likely to be introduced within next two years. Exactly what the new regulations will say and how they will be implemented is still unclear. Several participants at the Roundtable had concerns about the effectiveness of only relying on national or European legislation as a means to effect change, as this can be a blunt tool that is both slow and expensive to pass and implement. In addition, the difficulties of effective enforcement across the EU were discussed. However, it is a useful baseline to help drive additional progress through voluntary schemes.

### Behavioural Change

The current variation in farmer and vet attitudes, and often lack of knowledge and understanding of this issue was identified as a driver of bad practice. Changing existing behaviours through information, training and standardising practices is likely to go a long way to improve the situation. The participants raised a number of issues, including:

Firstly, no training or certification is currently required to administer medicines on a farm, in sharp contrast to for example pesticide application and machinery operation. Responsible Use of Medicines in Agriculture (RUMA) is preparing a training syllabus that can be delivered to anyone using medicines on farm. Veterinary practices should play a crucial role in delivering courses in line with the RUMA syllabus to their clients.

Secondly, while vets must ultimately take responsibility for prescribing antibiotics there is often pressure, or an expectation from some clients, that medicines can be picked up within a few hours of phoning through their request without further consultation with the vet. Vets should receive training and support from the veterinary practice/pharmacy to make the often-difficult decision to say 'no.' Participants were however in agreement that there were farmers and producers with a much more progressive outlook.

### System Change

One participant drew on experience to say there might be certain farming systems that are so reliant on antibiotics to operate that they perhaps should be discontinued or radically reformed. Unfortunately, there are sparse hard data available to help tease out such associations between the degree of antimicrobial use and efficiency in different systems, independent of other factors such as how well the farms are run.

Another element of system change is for some farmers to change their view and attitude toward their vets. Rather than simply viewing them as a source of medicines and the call of last resort, practice

would change if farmers viewed vets as business partners that can help in the development and design of production systems and prevention practices.

## REGULATING THE USE OF CRITICALLY IMPORTANT ANTIMICROBIALS (CIAs)

There was broad agreement at the Roundtable that CIAs should be treated as a special category of antimicrobials. However, there are some differences in the categorisation of CIAs between the approaches of the World Health Organisation (WHO), the World Organisation for Animal Health (OIE) and the US Food and Drug Administration (FDA, which can lead to confusion over the exact meaning of the term 'critically important.' Still, fluoroquinolones, 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins (only 3<sup>rd</sup> in the FDA list; 4<sup>th</sup> ranked lower at highly important) and macrolides are all assessed as critically important (and highest priority in the WHO list). Please see the complete lists at the links below:

- WHO list: [http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485_eng.pdf)
- OIE list: [http://www.oie.int/fileadmin/Home/eng/Our\\_scientific\\_expertise/docs/pdf/OIE\\_List\\_antimicrobials.pdf](http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/OIE_List_antimicrobials.pdf)
- FDA list – see Appendix A in <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf>

Regardless of the level of awareness and understanding of the role of CIAs, they may still be used in animal agriculture due to their effectiveness and suitability for use. Some participants expressed concern that if there were to be a complete ban on the use of CIAs in food-producing animals, options for some disease treatments may be limited, and potential consequences could include treatment failures with associated welfare and productivity costs. A compromise may need to be made to make CIAs the absolute last resort, with the inclusion of additional steps to ensure their responsible use.

## RETAILERS' POLICY AND PUBLIC MESSAGING

Antimicrobial resistance is high on retailers' agenda. However, it is unclear what exactly retailers can helpfully do to drive this issue forward, as retailers' actions are primarily motivated by initiatives which improve their competitiveness *vis a vis* customers and suppliers. The current language being used to describe this challenge scares consumers, and this could be the reason why the most prominent public messaging from retailers has been focused on claims of going 'antibiotics free.'

One participant argued that organic retailers might be less aware of the specifics around antimicrobial resistance because they often consider themselves uninvolved or unaffected by the debate. Furthermore, there was wide spread agreement that the rhetoric of 'antibiotics free' is a potentially dangerous, albeit powerful, message for consumers. To illustrate this point another participant raised the example of a US company that recently pledged to only use antibiotic-free chicken within a 5 year time-frame. This may only be possible when working with a large supplier that can maintain a sufficient source of antibiotic-free chicken, alongside 'conventional' chicken. This does not necessarily drive positive change in behaviours, and could even have detrimental effects for both animals (welfare impact of untreated disease), and producers themselves (decision-making around medicine use may not be driven by health and welfare concerns).

# MEASUREMENT

## CURRENT COMMON PRACTICE

The most reported measure of antibiotics use in the UK and Europe is milligram (mg) of antimicrobial ingredient per kilogram (kg) of bodyweight (mg/kg)<sup>1</sup>. For example a common measure used in poultry production is total weight of antibiotics administered over a lifetime relative to carcass weight. The Roundtable participants agreed that this, and other similar measures, may have serious shortcomings, potentially incentivising the wrong behaviours, including:

- Using more potent antibiotics (usually CIAs) = lower mg/kg
- Not completing prescribed course = lower mg/kg
- Treating younger animals = lower mg/kg (in the poultry example).

## PROPOSED NEW MEASURE

In humans, there is a defined daily dose (DDD) for a 70kg human established for each antimicrobial. Usage is described in terms of number of doses or number of treatment courses over a given time period. This standardisation enables comparisons of usage regardless of potency of the antimicrobial.

There was agreement amongst participants at the Roundtable that the reporting of antimicrobial use in food animals needs to be improved and standardised. The goal of a new measure is to enable demonstration of any reduction and/or change in use, as well as to make comparisons between species, countries, and over time.

One such approach presented at the Roundtable was to adapt the human DDD approach for each species of animals and for each antimicrobial. In turn a course dose can be defined for each antimicrobial in each species. By recording data on the amount of each antimicrobial prescribed, the species and production class (e.g. suckling piglet, weaner, finisher) for which it was prescribed, the number of doses, or number of courses, for each production class in each species over a given time period can be reported. Number of courses is probably the most relevant measure. Participants noted that one possible limitation of this approach could be related to the DDD not necessarily being equivalent to the actual prescribed or administered dose.

A move towards defined daily dose for animals (DDD<sub>animal</sub>) is likely to be agreed at the European level, although this may take several years. Mirroring an approach that has been used (and published) in other countries (e.g. Denmark, Netherlands, Germany), several participants argued that it would be feasible for the UK industry to start adopting and establishing a DDD<sub>animal</sub> in a much shorter timeframe. Even if the actual figures for DDD<sub>animal</sub> that will eventually be decided at European level are different, the data collected to facilitate measuring and analysing use will likely remain the same, and calculations can be relatively easily updated.

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<sup>1</sup> For clarification purposes, antibiotics may be used as a Metaphylaxis, referring to the treatment of a group of animals when clinical signs present in at least one animal, and as a Prophylaxis, meaning that a group of animals are treated when there is high suspicion of illness but absence of any clinical signs

## ISSUES TO CONSIDER

When considering the adoption of a new system for antimicrobial measures it is important to see this in association with other measures of food safety, productivity and welfare. It also important to assess what impact the new measure will have in changing stakeholders' behaviours. Participants highlighted that the following measures should not be allowed to move in a negative direction in order to reduce antimicrobial usage:

- Mortality rates and other welfare indicators
- Productivity indicators such as production costs, carcass quality etc.
- Microbial testing results e.g. *Salmonella*, *Campylobacter*

With standardisation and improvements in collection of prescription and usage data, the need for a cohesive database system within species, country or global regions, will be strengthened. Such a system does not currently exist in the UK. While the Veterinary Medicines Directorate (VMD) has discussed this requirement, funding may be an issue.

# WAYS FORWARD

## A POTENTIAL FRAMEWORK FOR RESPONSIBLE USE

Agreement emerged around a proposal presented by one participant to adapt Russell and Burch's (1959) 3Rs framework of **Replace, Reduce, Refine**, to help drive responsible use of antimicrobials. The concept has been used as an ethical framework since the late 1950's to address concerns about responsible use of animals for experimental scientific research. Below is an outline of what an adapted 3Rs framework could look like:

### Replace

Where currently antibiotics are the first line of attack, effort should be made to **replace** the need for their use, primarily through comprehensive disease prevention. Factors to consider include:

- Improved husbandry and management
- Nutrition
- Genetics
- Vaccines
- Immuno-modulants
- Biosecurity
- Training, knowledge and technology
- Farmer/producer/veterinarian attitude
- Quarantine
- Disease eradication programmes

### Reduce

Where antibiotics are commonly deployed, effort should be made to **reduce** their use. Factors to consider include:

- Develop and improve utilisation of diagnostics and sensitivity testing technology to target initial treatment in order to avoid treatment failures.
- Ensure antibiotics are administered correctly using properly maintained equipment, at the correct dosage for the correct duration by the correct route.
- Address lack of farmer training/certification/accreditation for the administration of antibiotics (akin to training and certification for pesticide use).
- Measure and analyse the use of antibiotics in a standardised manner (see "Proposed Measure" section above), to enable meaningful comparisons between production classes within species, between species, between regions and between countries. Measurement would also provide baselines against which any reductions could be measured.
- Change farmers' and vets' behaviours by highlighting good and bad practices from within and between sectors and countries (standardised measures could also assist with this). (Systems exist in the Netherlands and Denmark for example).

### Refine

Where antibiotics are needed, effort should be made to **refine** their use to ensure they are deployed as intelligently and effectively as possible. Factors to consider include:

- Optimise efficacy by reviewing current datasheet recommendations on dosage, duration and routes of administration
- Ensure correct drug selection in light of AMR concerns (e.g. special scrutiny of CIA use)
- Increase the visibility of information on labels relating to the category of antibiotic and its relative importance in human or veterinary medicine for example.
- Improve farmer training/certification/accreditation, as above

## USING AND COMMUNICATING THE 3Rs FRAMEWORK

There was enthusiasm for the opportunity to apply the 3Rs framework to each antimicrobial in order to assess how its use could be replaced, reduced and refined both now (using currently available information) and into the future (by addressing information gaps). The complementarity between the 3Rs framework and the proposed DDDanimal approach for measuring use of individual antimicrobials was also noted by the Roundtable. Participants also highlighted that the 3Rs framework does not preclude CIAs from being treated as a special category and/or being banned or restricted from use in food animals.

Participants agreed that the promotion, implementation and demonstration of the 3Rs approach to antimicrobial usage represent an opportunity for farmers and producers to take leadership in shaping the direction of this increasingly high-profile and important human health issue. Furthermore, the 3Rs were thought of as an appropriate approach for framing key public messages that are likely to resonate with consumers.

## NEXT STEPS

Participants at the Roundtable agreed the following three 'next steps' as a way to facilitate deeper engagement and involve more relevant actors in this important challenge facing animal agriculture:

- 1) **Agree a path for establishing a new and standardised measure for antibiotic use** that can be implemented at producer level, and direct change at national and regional levels. This requires identifying the most appropriate outcome measures that demonstrate reductions and changes in use, while maintaining productivity, animal health and welfare standards.
- 2) **Agree on a common understanding of the term 'Critically Important Antimicrobials (CIA)';** and define the correct categories of antimicrobials the term should apply to in the context of use in food-producing animals.
- 3) **Develop a 3Rs framework of Replace, Reduce, Refine for the responsible use of antimicrobials** that can be implemented throughout the supply chain (vets, farmers, producers, retailers and the pharmaceutical industry), and communicated to consumers.



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